

SEQUENCE LISTING

(1) GENERAL INFORMATION:

(i) APPLICANT:

(A) NAME: NOVO NORDISK
 (B) STREET: Novo Alle
 (C) CITY: Bagsvaerd
 (E) COUNTRY: Denmark
 (F) POSTAL CODE (ZIP): DK-2800
 (G) TELEPHONE: +45 44 44 88 88
 (H) TELEFAX: +45 44 49 05 55

(ii) TITLE OF INVENTION: LACCASE MUTANTS

(iii) NUMBER OF SEQUENCES: 10

(iv) COMPUTER READABLE FORM:

(A) MEDIUM TYPE: Floppy disk
 (B) COMPUTER: IBM PC compatible
 (C) OPERATING SYSTEM: PC-DOS/MS-DOS
 (D) SOFTWARE: PatentIn Release #1.0, Version #1.30 (EPO)

(2) INFORMATION FOR SEQ ID NO: 1:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 539 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 1:

Met	Phe	Lys	Asn	Leu	Leu	Ser	Phe	Ala	Leu	Leu	Ala	Ile	Ser	Val	Ala	1	5	10	15
Asn	Ala	Gln	Ile	Val	Asn	Ser	Val	Asp	Thr	Met	Thr	Leu	Thr	Asn	Ala	20	25	30	
Asn	Val	Ser	Pro	Asp	Gly	Phe	Thr	Arg	Ala	Gly	Ile	Leu	Val	Asn	Gly	35	40	45	
Val	His	Gly	Pro	Leu	Ile	Arg	Gly	Gly	Lys	Asn	Asp	Asn	Phe	Glu	Leu	50	55	60	
Asn	Val	Val	Asn	Asp	Leu	Asp	Asn	Pro	Thr	Met	Leu	Arg	Pro	Thr	Ser	65	70	75	80
Ile	His	Trp	His	Gly	Leu	Phe	Gln	Arg	Gly	Thr	Asn	Trp	Ala	Asp	Gly	85	90	95	
Ala	Asp	Gly	Val	Asn	Gln	Cys	Pro	Ile	Ser	Pro	Gly	His	Ala	Phe	Leu	100	105	110	
Tyr	Lys	Phe	Thr	Pro	Ala	Gly	His	Ala	Gly	Thr	Phe	Trp	Tyr	His	Ser	115	120	125	
His	Phe	Gly	Thr	Gln	Tyr	Cys	Asp	Gly	Leu	Arg	Gly	Pro	Met	Val	Ile	130	135	140	
Tyr	Asp	Asp	Asn	Asp	Pro	His	Ala	Ala	Leu	Tyr	Asp	Glu	Asp	Asp	Glu	145	150	155	160
Asn	Thr	Ile	Ile	Thr	Leu	Ala	Asp	Trp	Tyr	His	Ile	Pro	Ala	Pro	Ser				

	165										170					175				
5	Ile	Gln	Gly	Ala	Ala	Gln	Pro	Asp	Ala	Thr	Leu	Ile	Asn	Gly	Lys	Gly				
				180					185					190						
	Arg	Tyr	Val	Gly	Gly	Pro	Ala	Ala	Glu	Leu	Ser	Ile	Val	Asn	Val	Glu				
			195					200					205							
10	Gln	Gly	Lys	Lys	Tyr	Arg	Met	Arg	Leu	Ile	Ser	Leu	Ser	Cys	Asp	Pro				
		210					215					220								
	Asn	Trp	Gln	Phe	Ser	Ile	Asp	Gly	His	Glu	Leu	Thr	Ile	Ile	Glu	Val				
	225					230					235				240					
15	Asp	Gly	Gln	Leu	Thr	Glu	Pro	His	Thr	Val	Asp	Arg	Leu	Gln	Ile	Phe				
					245					250					255					
	Thr	Gly	Gln	Arg	Tyr	Ser	Phe	Val	Leu	Asp	Ala	Asn	Gln	Pro	Val	Asp				
				260					265					270						
20	Asn	Tyr	Trp	Ile	Arg	Ala	Gln	Pro	Asn	Lys	Gly	Arg	Asn	Gly	Leu	Ala				
			275					280					285							
	Gly	Thr	Phe	Ala	Asn	Gly	Val	Asn	Ser	Ala	Ile	Leu	Arg	Tyr	Ala	Gly				
25		290					295					300								
	Ala	Ala	Asn	Ala	Asp	Pro	Thr	Thr	Ser	Ala	Asn	Pro	Asn	Pro	Ala	Gln				
	305					310					315					320				
30	Leu	Asn	Glu	Ala	Asp	Leu	His	Ala	Leu	Ile	Asp	Pro	Ala	Ala	Pro	Gly				
					325					330					335					
	Ile	Pro	Thr	Pro	Gly	Ala	Ala	Asp	Val	Asn	Leu	Arg	Phe	Gln	Leu	Gly				
35				340					345					350						
	Phe	Ser	Gly	Gly	Arg	Phe	Thr	Ile	Asn	Gly	Thr	Ala	Tyr	Glu	Ser	Pro				
			355					360					365							
40	Ser	Val	Pro	Thr	Leu	Leu	Gln	Ile	Met	Ser	Gly	Ala	Gln	Ser	Ala	Asn				
		370					375					380								
	Asp	Leu	Leu	Pro	Ala	Gly	Ser	Val	Tyr	Glu	Leu	Pro	Arg	Asn	Gln	Val				
	385					390					395					400				
45	Val	Glu	Leu	Val	Val	Pro	Ala	Gly	Val	Leu	Gly	Gly	Pro	His	Pro	Phe				
					405					410					415					
	His	Leu	His	Gly	His	Ala	Phe	Ser	Val	Val	Arg	Ser	Ala	Gly	Ser	Ser				
				420					425					430						
50	Thr	Tyr	Asn	Phe	Val	Asn	Pro	Val	Lys	Arg	Asp	Val	Val	Ser	Leu	Gly				
			435					440					445							
	Val	Thr	Gly	Asp	Glu	Val	Thr	Ile	Arg	Phe	Val	Thr	Asp	Asn	Pro	Gly				
55		450					455					460								
	Pro	Trp	Phe	Phe	His	Cys	His	Ile	Glu	Phe	His	Leu	Met	Asn	Gly	Leu				
	465					470					475					480				
60	Ala	Ile	Val	Phe	Ala	Glu	Asp	Met	Ala	Asn	Thr	Val	Asp	Ala	Asn	Asn				
					485					490					495					
	Pro	Pro	Val	Glu	Trp	Ala														

Gly Phe Ser Ala Lys Phe Arg Arg Glu Gly Leu
530 535

5 (2) INFORMATION FOR SEQ ID NO: 2:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 499 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 2:

Gly Ile Gly Pro Val Ala Asp Leu Thr Ile Thr Asn Ala Ala Val Ser
1 5 10 15
Pro Asp Gly Phe Ser Arg Gln Ala Val Val Val Asn Gly Gly Thr Pro
20 25 30
Gly Pro Leu Ile Thr Gly Asn Met Gly Asp Arg Phe Gln Leu Asn Val
25 35 40 45
Ile Asp Asn Leu Thr Asn His Thr Met Leu Lys Ser Thr Ser Ile His
50 55 60
Trp His Gly Phe Phe Gln Lys Gly Thr Asn Trp Ala Asp Gly Pro Ala
65 70 75 80
Phe Ile Asn Gln Cys Pro Ile Ser Ser Gly His Ser Phe Leu Tyr Asp
85 90 95
Phe Gln Val Pro Asp Gln Ala Gly Thr Phe Trp Tyr His Ser His Leu
100 105 110
Ser Thr Gln Tyr Cys Asp Gly Leu Arg Gly Pro Phe Val Val Tyr Asp
115 120 125
Pro Asn Asp Pro Ala Ala Asp Leu Tyr Asp Val Asp Asn Asp Asp Thr
130 135 140
Val Ile Thr Leu Val Asp Trp Tyr His Val Ala Ala Lys Leu Gly Pro
145 150 155 160
Ala Phe Pro Leu Gly Ala Asp Ala Thr Leu Ile Asn Gly Lys Gly Arg
165 170 175
Ser Pro Ser Thr Thr Thr Ala Asp Leu Ser Val Ile Ser Val Thr Pro
180 185 190
Gly Lys Arg Tyr Arg Phe Arg Leu Val Ser Leu Ser Cys Asp Pro Asn
195 200 205
Tyr Thr Phe Ser Ile Asp Gly His Asn Met Thr Ile Ile Glu Thr Asp
210 215 220
Ser Ile Asn Thr Ala Pro Leu Val Val Asp Ser Ile Gln Ile Phe Ala
225 230 235 240
Ala Gln Arg Tyr Ser Phe Val Leu Glu Ala Asn Gln Ala Val Asp Asn
245 250 255
Tyr Trp Ile Arg Ala Asn Pro Asn Phe Gly Asn Val Gly Phe Thr Gly
260 265 270

120

Gly Ile Asn Ser Ala Ile Leu Arg Tyr Asp Gly Ala Ala Ala Val Glu
 275 280 285
 Pro Thr Thr Thr Gln Thr Thr Ser Thr Ala Pro Leu Asn Glu Val Asn
 290 295 300
 Leu His Pro Leu Val Thr Thr Ala Val Pro Gly Ser Pro Val Ala Gly
 305 310 315 320
 Gly Val Asp Leu Ala Ile Asn Met Ala Phe Asn Phe Asn Gly Thr Asn
 325 330 335
 Phe Phe Ile Asn Gly Ala Ser Phe Thr Pro Pro Thr Val Pro Val Leu
 340 345 350
 Leu Gln Ile Ile Ser Gly Ala Gln Asn Ala Gln Asp Leu Leu Pro Ser
 355 360 365
 Gly Ser Val Tyr Ser Leu Pro Ser Asn Ala Asp Ile Glu Ile Ser Phe
 370 375 380
 Pro Ala Thr Ala Ala Ala Pro Gly Ala Pro His Pro Phe His Leu His
 385 390 395 400
 Gly His Ala Phe Ala Val Val Arg Ser Ala Gly Ser Thr Val Tyr Asn
 405 410 415
 Tyr Asp Asn Pro Ile Phe Arg Asp Val Val Ser Thr Gly Thr Pro Ala
 420 425 430
 Ala Gly Asp Asn Val Thr Ile Arg Phe Arg Thr Asp Asn Pro Gly Pro
 435 440 445
 Trp Phe Leu His Cys His Ile Asp Phe His Leu Glu Ala Gly Phe Ala
 450 455 460
 Val Val Phe Ala Glu Asp Ile Pro Asp Val Ala Ser Ala Asn Pro Val
 465 470 475 480
 Pro Gln Ala Trp Ser Asp Leu Cys Pro Thr Tyr Asp Ala Leu Asp Pro
 485 490 495
 Ser Asp Gln

(2) INFORMATION FOR SEQ ID NO: 3:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 499 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 3:

Ala Ile Gly Pro Val Ala Ser Leu Val Val Ala Asn Ala Pro Val Ser
 1 5 10 15
 Pro Asp Gly Phe Leu Arg Asp Ala Ile Val Val Asn Gly Val Val Pro
 20 25 30
 Ser Pro Leu Ile Thr Gly Lys Lys Gly Asp Arg Phe Gln Leu Asn Val
 35 40 45
 Val Asp Thr Leu Thr Asn His Ser Met Leu Lys Ser Thr Ser Ile His

50 55 60

Trp His Gly Phe Phe Gln Ala Gly Thr Asn Trp Ala Glu Gly Pro Ala
65 70 75 80

5 Phe Val Asn Gln Cys Pro Ile Ala Ser Gly His Ser Phe Leu Tyr Asp
85 90 95

10 Phe His Val Pro Asp Gln Ala Gly Thr Phe Trp Tyr His Ser His Leu
100 105 110

Ser Thr Gln Tyr Cys Asp Gly Leu Arg Gly Pro Phe Val Val Tyr Asp
115 120 125

15 Pro Lys Asp Pro His Ala Ser Arg Tyr Asp Val Asp Asn Glu Ser Thr
130 135 140

Val Ile Thr Leu Thr Asp Trp Tyr His Thr Ala Ala Arg Leu Gly Pro
145 150 155 160

20 Lys Phe Pro Leu Gly Ala Asp Ala Thr Leu Ile Asn Gly Leu Gly Arg
165 170 175

25 Ser Ala Ser Thr Pro Thr Ala Ala Leu Ala Val Ile Asn Val Gln His
180 185 190

Gly Lys Arg Tyr Arg Phe Arg Leu Val Ser Ile Ser Cys Asp Pro Asn
195 200 205

30 Tyr Thr Phe Ser Ile Asp Gly His Asn Leu Thr Val Ile Glu Val Asp
210 215 220

Gly Ile Asn Ser Gln Pro Leu Leu Val Asp Ser Ile Gln Ile Phe Ala
225 230 235 240

35 Ala Gln Arg Tyr Ser Phe Val Leu Asn Ala Asn Gln Thr Val Gly Asn
245 250 255

40 Tyr Trp Val Arg Ala Asn Pro Asn Phe Gly Thr Val Gly Phe Ala Gly
260 265 270

Gly Ile Asn Ser Ala Ile Leu Arg Tyr Gln Gly Ala Pro Val Ala Glu
275 280 285

45 Pro Thr Thr Thr Gln Thr Pro Ser Val Ile Pro Leu Ile Glu Thr Asn
290 295 300

Leu His Pro Leu Ala Arg Met Pro Val Pro Gly Ser Pro Thr Pro Gly
305 310 315 320

50 Gly Val Asp Lys Ala Leu Asn Leu Ala Phe Asn Phe Asn Gly Thr Asn
325 330 335

Phe Phe Ile Asn Asn Ala Thr Phe Thr Pro Pro Thr Val Pro Val Leu
340 345 350

55 Leu Gln Ile Leu Ser Gly Ala Gln Thr Ala Gln Asp Leu Leu Pro Ala
355 360 365

60 Gly Ser Val Tyr Pro Leu Pro Ala His Ser Thr Ile Glu Ile Thr Leu
370 375 380

Pro Ala Thr Ala Leu Ala Pro Gly Ala Pro His Pro Phe His Leu His
385 390 395 400

Gly His Ala Phe Ala Val Val Arg Ser Ala Gly Ser Thr Thr Tyr Asn
405 410 415

Tyr Asn Asp Pro Ile Phe Arg Asp Val Val Ser Thr Gly Thr Pro Ala
 420 425 430
 5 Ala Gly Asp Asn Val Thr Ile Arg Phe Gln Thr Asp Asn Pro Gly Pro
 435 440 445
 Trp Phe Leu His Cys His Ile Asp Phe His Leu Asp Ala Gly Phe Ala
 450 455 460
 10 Ile Val Phe Ala Glu Asp Val Ala Asp Val Lys Ala Ala Asn Pro Val
 465 470 475 480
 15 Pro Lys Ala Trp Ser Asp Leu Cys Pro Ile Tyr Asp Gly Leu Ser Glu
 485 490 495
 Ala Asn Gln

20 (2) INFORMATION FOR SEQ ID NO: 4:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 548 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 4:

Met His Thr Phe Leu Arg Ser Thr Ala Leu Val Val Ala Gly Leu Ser
 1 5 10 15
 35 Ala Arg Ala Leu Ala Ser Ile Gly Pro Val Thr Asp Phe His Ile Val
 20 25 30
 40 Asn Ala Ala Val Ser Pro Asp Gly Phe Ser Arg Gln Ala Val Leu Ala
 35 40 45
 Glu Gly Val Phe Pro Gly Pro Leu Ile Ala Gly Asn Lys Gly Asp Asn
 50 55 60
 45 Phe Gln Ile Asn Val Ile Asp Glu Leu Thr Asn Ala Thr Met Leu Lys
 65 70 75 80
 Thr Thr Thr Ile His Trp His Gly Phe Phe Gln His Gly Thr Asn Trp
 85 90 95
 50 Ala Asp Gly Pro Ala Phe Ile Asn Gln Cys Pro Ile Ala Ser Gly Asp
 100 105 110
 55 Ser Phe Leu Tyr Asn Phe Gln Val Pro Asp Gln Ala Gly Thr Phe Trp
 115 120 125
 Tyr His Ser His Leu Ser Thr Gln Tyr Cys Asp Gly Leu Arg Gly Pro
 130 135 140
 60 Phe Val Val Tyr Asp Pro Ala Asp Pro Tyr Leu Asp Gln Tyr Asp Val
 145 150 155 160
 Asp Asp Asp Ser Thr Val Ile Thr Leu Ala Asp Trp Tyr His Thr Ala
 165 170 175
 65 Ala Arg Leu Gly Ser Pro Phe Pro Ala Ala Asp Thr Thr Leu Ile Asn
 180 185 190

Gly Leu Gly Arg Cys Gly Glu Ala Gly Cys Pro Val Ser Asp Leu Ala
 195 200 205
 5 Val Ile Ser Val Thr Lys Gly Lys Arg Tyr Arg Phe Arg Leu Val Ser
 210 215 220
 Ile Ser Cys Asp Ser Phe Phe Thr Phe Ser Ile Asp Gly His Ser Leu
 225 230 235 240
 10 Asn Val Ile Glu Val Asp Ala Thr Asn His Gln Pro Leu Thr Val Asp
 245 250 255
 Glu Leu Thr Ile Tyr Ala Gly Gln Arg Tyr Ser Phe Ile Leu Thr Ala
 260 265 270
 15 Asp Gln Asp Val Asp Asn Tyr Trp Ile Arg Ala Asn Pro Gly Ile Gly
 275 280 285
 Ile Thr Thr Gly Phe Ala Gly Gly Ile Asn Ser Ala Ile Leu Arg Tyr
 290 295 300
 20 Asp Gly Ala Asp Val Val Glu Pro Thr Thr Thr Gln Ala Thr Ser Pro
 305 310 315 320
 Val Val Leu Ser Glu Ser Asn Leu Ala Pro Leu Thr Asn Ala Ala Ala
 325 330 335
 25 Pro Gly Leu Pro Glu Val Gly Gly Val Asp Leu Ala Leu Asn Phe Asn
 340 345 350
 30 Leu Thr Phe Asp Gly Pro Ser Leu Lys Phe Gln Ile Asn Gly Val Thr
 355 360 365
 Phe Val Pro Pro Thr Val Pro Val Leu Leu Gln Ile Leu Ser Gly Ala
 370 375 380
 35 Gln Ser Ala Ala Asp Leu Leu Pro Ser Gly Ser Val Tyr Ala Leu Pro
 385 390 395 400
 40 Ser Asn Ala Thr Ile Glu Leu Ser Leu Pro Ala Gly Ala Leu Gly Gly
 405 410 415
 Pro His Pro Phe His Leu His Gly His Thr Phe Ser Val Val Arg Pro
 420 425 430
 45 Ala Gly Ser Thr Thr Tyr Asn Tyr Val Asn Pro Val Gln Arg Asp Val
 435 440 445
 Val Ser Ile Gly Asn Thr Gly Asp Asn Val Thr Ile Arg Phe Asp Thr
 450 455 460
 50 Asn Asn Pro Gly Pro Trp Phe Leu His Cys His Ile Asp Trp His Leu
 465 470 475 480
 55 Glu Ala Ala Leu Pro Leu Ser Ser Leu Arg Thr Ser Leu Thr Leu Arg
 485 490 495
 Pro Leu Thr Leu Ser Pro Arg Thr Gly Pro Thr Cys Ala Leu Ser Thr
 500 505 510
 60 Thr Leu Trp Thr His Leu Ile Thr Ser Gly Phe Ala Ser Ile Ile Gln
 515 520 525
 65 Trp Met Met Gly Gly Asn Gly Leu Phe Ala Pro His Ala Leu Ser Phe
 530 535 540
 Leu Gly Ser Gln

~~545~~

(2) INFORMATION FOR SEQ ID NO: 5:

5 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 529 amino acids

(B) TYPE: amino acid

(C) \STRANDEDNESS: single

(D) TOPOLOGY: linear

10 (ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 5:

Met Leu Ser Ser Ile Thr Leu Leu Pro Leu Leu Ala Ala Val Ser Thr
1 5 10 15

20 Pro Ala Phe Ala Val Arg Asn Tyr Lys Phe Asp Ile Lys Asn Val
20 25 30

Asn Val Ala Pro Asp Gly Phe Gln Arg Ser Ile Val Ser Val Asn Gly
35 40 45

25 Leu Val Pro Gly Thr Leu Ile Thr Ala Asn Lys Gly Asp Thr Leu Arg
 50 55 60

Ile Asn Val Thr Asn Gln / Leu Thr Asp Pro Ser Met Arg Arg Ala Thr
65 70 75 80

Thr Ile His Trp His Gly Leu Phe Gln Ala Thr Thr Ala Asp Glu Asp
85 90 95

35 Gly Pro Ala Phe Val Thr Gln Cys Pro Ile Ala Gln Asn Leu Ser Tyr
100 105 110

Thr Tyr Glu Ile Pro Leu Arg Gly Gln Thr Gly Thr Met Trp Tyr His
115 120 125

40 Ala His Leu Ala Ser Gln Tyr Val Asp Gly Leu Arg Gly Pro Leu Val
130 135 140

Ile Tyr Asp Pro Asn Asp Pro His Lys Ser Arg Tyr Asp Val Asp Asp
145 150 155 160

Ala Ser Thr Val Val Met Leu Glu Asp Trp Tyr His Thr Pro Ala Pro
165 170 175

50 Val Leu Glu Lys Gln Met Phe Ser Thr Asn Asn Thr Ala Leu Leu Ser
180 185 190

Pro Val Pro Asp Ser Gly Leu Ile Asn Gly Lys Gly Arg Tyr Val Gly
195 200 205

55 Gly Pro Ala Val Pro Arg Ser Val Ile Asn Val Lys Arg Gly Lys Arg
210 215 220

Tyr Arg Leu Arg Val Ile Asn Ala Ser Ala Ile Gly Ser Phe Thr Phe
225 230 235 240

00 Ser Ile Glu Gly His Ser Leu Thr Val Ile Glu Ala Asp Gly Ile Leu
245 250 255

His Gln Pro Leu Ala Val Asp Ser Phe Gln Ile Tyr Ala Gly Gln Arg
65 260 265 270

Tyr Ser Val Ile Val Glu Ala Asn Gln Thr Ala Ala Asn Tyr Trp Ile
275 280 285

Arg Ala Pro Met Thr Val Ala Gly Ala Gly Thr Asn Ala Asn Leu Asp
 290 295 300
 5 Pro Thr Asn Val Phe Ala Val Leu His Tyr Glu Gly Ala Pro Asn Ala
 305 310 315 320
 Glu Pro Thr Thr Glu Gln Gly Ser Ala Ile Gly Thr Ala Leu Val Glu
 325 330 335
 10 Glu Asn Leu His Ala Leu Ile Asn Pro Gly Ala Pro Gly Gly Ser Ala
 340 345 350
 15 Pro Ala Asp Val Ser Leu Asn Leu Ala Ile Gly Arg Ser Thr Val Asp
 355 360 365
 Gly Ile Leu Arg Phe Thr Phe Asn Asn Ile Lys Tyr Glu Ala Pro Ser
 370 375 380
 20 Leu Pro Thr Leu Leu Lys Ile Leu Ala Asn Asn Ala Ser Asn Asp Ala
 385 390 395 400
 Asp Phe Thr Pro Asn Glu His Thr Ile Val Leu Pro His Asn Lys Val
 405 410 415
 25 Ile Glu Leu Asn Ile Thr Gly Gly Ala Asp His Pro Ile His Leu His
 420 425 430
 Gly His Val Phe Asp Ile Val Lys Ser Leu Gly Gly Thr Pro Asn Tyr
 435 440 445
 30 Val Asn Pro Pro Arg Arg Asp Val Val Arg Val Gly Gly Thr Gly Val
 450 455 460
 35 Val Leu Arg Phe Lys Thr Asp Asn Pro Gly Pro Trp Phe Val His Cys
 465 470 475 480
 His Ile Asp Trp His Leu Glu Ala Gly Leu Ala Leu Val Phe Ala Glu
 485 490 495
 40 Ala Pro Ser Gln Ile Arg Gln Gly Val Gln Ser Val Gln Pro Asn Asn
 500 505 510
 45 Ala Trp Asn Gln Leu Cys Pro Lys Tyr Ala Ala Leu Pro Pro Asp Leu
 515 520 525
 Gln

50 (2) INFORMATION FOR SEQ ID NO: 6:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 599 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 6:

Met Ala Arg Ser Thr Thr Ser Leu Phe Ala Leu Ser Leu Val Ala Ser
 1 5 10 15
 65 Ala Phe Ala Arg Val Val Asp Tyr Gly Phe Asp Val Ala Asn Gly Ala
 20 25 30
 Val Ala Pro Asp Gly Val Thr Arg Asn Ala Val Leu Val Asn Gly Arg

405 410 415
 Gly Gly Ser Arg Pro Ala Asp Val Val Val Pro Leu Asp Phe Gly Leu
 420 425 430
 5 Asn Phe Ala Asn Gly Leu Trp Thr Ile Asn Asn Val Ser Tyr Ser Pro
 435 440 445
 10 Pro Asp Val Pro Thr Leu Leu Lys Ile Leu Thr Asp Lys Asp Lys Val
 450 455 460
 Asp Ala Ser Asp Phe Thr Ala Asp Glu His Thr Tyr Ile Leu Pro Lys
 465 470 475 480
 15 Asn Gln Val Val Glu Leu His Ile Lys Gly Gln Ala Leu Gly Ile Val
 485 490 495
 His Pro Leu His Leu His Gly His Ala Phe Asp Val Val Gln Phe Gly
 500 505 510
 20 Asp Asn Ala Pro Asn Tyr Val Asn Pro Pro Arg Arg Asp Val Val Gly
 515 520 525
 Val Thr Asp Ala Gly Val Arg Ile Gln Phe Arg Thr Asp Asn Pro Gly
 530 535 540
 25 Pro Trp Phe Leu His Cys His Ile Asp Trp His Leu Glu Glu Gly Phe
 545 550 555 560
 30 Ala Met Val Phe Ala Glu Ala Pro Glu Asp Ile Lys Lys Gly Ser Gln
 565 570 575
 Ser Val Lys Pro Asp Gly Gln Trp Lys Lys Leu Cys Glu Lys Tyr Glu
 580 585 590
 35 Lys Leu Pro Glu Ala Leu Gln
 595

(2) INFORMATION FOR SEQ ID NO: 7:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 572 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 7:

Met Ala Arg Thr Thr Phe Leu Val Ser Val Ser Leu Phe Val Ser Ala
 1 5 10 15
 55 Val Leu Ala Arg Thr Val Glu Tyr Asn Leu Lys Ile Ser Asn Gly Lys
 20 25 30
 Ile Ala Pro Asp Gly Val Glu Arg Asp Ala Thr Leu Val Asn Gly Gly
 35 40 45
 60 Tyr Pro Gly Pro Leu Ile Phe Ala Asn Lys Gly Asp Thr Leu Lys Val
 50 55 60
 65 Lys Val Gln Asn Lys Leu Thr Asn Pro Asp Met Tyr Arg Thr Thr Ser
 65 70 75 80
 Ile His Trp His Gly Leu Leu Gln His Arg Asn Ala Asp Asp Asp Gly
 85 90 95

5 Pro Ala Phe Val Thr Gln Cys Pro Ile Val Pro Gln Ala Ser Tyr Thr
 100 105 110
 Tyr Thr Met Pro Leu Gly Asp Gln Thr Gly Thr Tyr Trp Tyr His Ser
 115 120 125
 10 His Leu Ser Ser Gln Tyr Val Asp Gly Leu Arg Gly Pro Leu Val Ile
 130 135 140
 Tyr Asp Pro Lys Asp Pro His Arg Arg Leu Tyr Asp Ile Asp Asp Glu
 145 150 155 160
 15 Lys Thr Val Leu Ile Ile Gly Asp Trp Tyr His Thr Ser Ser Lys Ala
 165 170 175
 Ile Leu Ala Thr Gly Asn Ile Thr Leu Gln Gln Pro Asp Ser Ala Thr
 180 185 190
 20 Ile Asn Gly Lys Gly Arg Phe Asp Pro Asp Asn Thr Pro Ala Asn Pro
 195 200 205
 Asn Thr Leu Tyr Thr Leu Lys Val Lys Arg Gly Lys Arg Tyr Arg Leu
 210 215 220
 25 Arg Val Ile Asn Ser Ser Ala Ile Ala Ser Phe Arg Met Ser Ile Gln
 225 230 235 240
 Gly His Lys Met Thr Val Ile Ala Ala Asp Gly Val Ser Thr Lys Pro
 245 250 255
 30 Tyr Gln Val Asp Ser Phe Asp Ile Leu Ala Gly Gln Arg Ile Asp Ala
 260 265 270
 35 Val Val Glu Ala Asn Gln Glu Pro Asp Thr Tyr Trp Ile Asn Ala Pro
 275 280 285
 Leu Thr Asn Val Ala Asn Lys Thr Ala Gln Ala Leu Leu Ile Tyr Glu
 290 295 300
 40 Asp Asp Arg Arg Pro Tyr His Pro Pro Lys Gly Pro Tyr Arg Lys Trp
 305 310 315 320
 45 Ser Val Ser Glu Ala Ile Ile Lys Tyr Trp Lys His Lys His Gly Arg
 325 330 335
 Gly Leu Leu Ser Gly His Gly Gly Leu Lys Ala Arg Met Met Glu Gly
 340 345 350
 50 Ser Leu His Leu His Gly Arg Arg Asp Ile Val Lys Arg Gln Asn Glu
 355 360 365
 Thr Thr Thr Val Val Met Asp Glu Thr Lys Leu Val Pro Leu Glu His
 370 375 380
 55 Pro Gly Ala Ala Cys Gly Ser Lys Pro Ala Asp Leu Val Ile Asp Leu
 385 390 395 400
 60 Thr Phe Gly Val Asn Phe Thr Thr Gly His Trp Met Ile Asn Gly Ile
 405 410 415
 Pro His Lys Ser Pro Asp Met Pro Thr Leu Leu Lys Ile Leu Thr Asp
 420 425 430
 65 Thr Asp Gly Val Thr Glu Ser Asp Phe Thr Gln Pro Glu His Thr Ile
 435 440 445

Ile Leu Pro Lys Asn Lys Cys Val Glu Phe Asn Ile Lys Gly Asn Ser
450 455 460

5 Gly Leu Gly Ile Val His Pro Ile His Leu His Gly His Thr Phe Asp
465 470 475 480

Val Val Gln Phe Gly Asn Asn Pro Pro Asn Tyr Val Asn Pro Pro Arg
485 490 495

10 Arg Asp Val Val Gly Ala Thr Asp Glu Gly Val Arg Phe Gln Phe Lys
500 505 510

Thr Asp Asn Pro Gly Pro Trp Phe Leu His Cys His Ile Asp Trp His
515 520 525

15 Leu Glu Glu Gly Phe Ala Met Val Phe Ala Glu Ala Pro Glu Ala Ile
530 535 540

Lys Gly Gly Pro Lys Ser Val Pro Val Asp Arg Gln Trp Lys Asp Leu
20 545 550 555 560

Cys Arg Lys Tyr Gly Ser Leu Pro Ala Gly Phe Leu
565 570

25 (2) INFORMATION FOR SEQ ID NO: 8:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 575 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 8:

Met Ala Arg Thr Thr Phe Leu Val Ser Val Ser Leu Phe Val Ser Ala
1 5 10 15

Val Leu Ala Arg Thr Val Glu Tyr Gly Leu Lys Ile Ser Asp Gly Glu
20 25 30

45 Ile Ala Pro Asp Gly Val Lys Arg Asn Ala Thr Leu Val Asn Gly Gly
35 40 45

Tyr Pro Gly Pro Leu Ile Phe Ala Asn Lys Gly Asp Thr Leu Lys Val
50 55 60

50 Lys Val Gln Asn Lys Leu Thr Asn Pro Glu Met Tyr Arg Thr Thr Ser
65 70 75 80

Ile His Trp His Gly Leu Leu Gln His Arg Asn Ala Asp Asp Asp Gly
85 90 95

Pro Ser Phe Val Thr Gln Cys Pro Ile Val Pro Arg Glu Ser Tyr Thr
100 105 110

60 Tyr Thr Ile Pro Leu Asp Asp Gln Thr Gly Thr Tyr Trp Tyr His Ser
115 120 125

His Leu Ser Ser Gln Tyr Val Asp Gly Leu Arg Gly Pro Leu Val Ile
130 135 140

65 Tyr Pro Lys Asp Pro His Arg Arg Leu Tyr Asp Val Asp Asp Glu Lys
145 150 155 160

Thr Val Leu Ile Ile Gly Asp Trp Tyr His Glu Ser Ser Lys ~~Ala~~ Ile

Leu Glu Glu Gly Phe Ala Met Val Phe Ala Glu Ala Pro Glu Ala Val
530 535 540

Lys Gly Gly Pro Lys Ser Val Ala Val Asp Ser Gln Trp Glu Gly Leu
545 550 555 560

Cys Gly Lys Tyr Asp Asn Trp Leu Lys Ser Asn Pro Gly Gln Leu
565 570 575

(2) INFORMATION FOR SEQ ID NO: 9:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 616 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 9:

Met Lys Arg Phe Phe Ile Asn Ser Leu Leu Leu Ala Gly Leu Leu
1 5 10 15

Asn Ser Gly Ala Leu Ala Ala Pro Ser Thr His Pro Arg Ser Asn Pro
20 25 30

Asp Ile Leu Leu Glu Arg Asp Asp His Ser Leu Thr Ser Arg Gln Gly
35 40 45

Ser Cys His Ser Pro Ser Asn Arg Ala Cys Trp Cys Ser Gly Phe Asp
50 55 60

Ile Asn Thr Asp Tyr Glu Thr Lys Thr Pro Asn Thr Gly Val Val Arg
65 70 75 80

Arg Tyr Thr Phe Asp Ile Thr Glu Val Asp Asn Arg Pro Gly Pro Asp
85 90 95

Gly Val Ile Lys Glu Lys Leu Met Leu Ile Asn Asp Lys Leu Leu Gly
100 105 110

Pro Thr Val Phe Ala Asn Trp Gly Asp Thr Ile Glu Val Thr Val Asn
115 120 125

Asn His Leu Arg Thr Asn Gly Thr Ser Ile His Trp His Gly Leu His
130 135 140

Gln Lys Gly Thr Asn Tyr His Asp Gly Ala Asn Gly Val Thr Glu Cys
145 150 155 160

Pro Ile Pro Pro Gly Gly Ser Arg Val Tyr Ser Phe Arg Ala Arg Gln
165 170 175

Tyr Gly Thr Ser Trp Tyr His Ser His Phe Ser Ala Gln Tyr Gly Asn
180 185 190

Gly Val Ser Gly Ala Ile Gln Ile Asn Gly Pro Ala Ser Leu Pro Tyr
195 200 205

Asp Ile Asp Leu Gly Val Leu Pro Leu Xaa Asp Trp Tyr Tyr Lys Ser
210 215 220

Ala Asp Gln Leu Val Ile Glu Thr Leu Xaa Lys Gly Asn Ala Pro Phe
225 230 235 240

002001-05000000

595

600

605

Leu Lys Gln Arg Arg Trp Asp Ala
610 615

(2) INFORMATION FOR SEQ ID NO: 10:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 573 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 10:

Gln Gln Ser Cys Asn Thr Pro Ser Asn Arg Ala Cys Trp Thr Asp Gly
1 5 10 15
Tyr Asp Ile Asn Thr Asp Tyr Glu Val Asp Ser Pro Asp Thr Gly Val
20 25 30
Val Arg Pro Tyr Thr Leu Thr Leu Thr Glu Val Asp Asn Trp Thr Gly
35 40 45
Pro Asp Gly Val Val Lys Glu Lys Val Met Leu Val Asn Asn Ser Ile
50 55 60
Ile Gly Pro Thr Ile Phe Ala Asp Trp Gly Asp Thr Ile Gln Val Thr
65 70 75 80
Val Ile Asn Asn Leu Glu Thr Asn Gly Thr Ser Ile His Trp His Gly
85 90 95
Leu His Gln Lys Gly Thr Asn Leu His Asp Gly Ala Asn Gly Ile Thr
100 105 110
Glu Cys Pro Ile Pro Pro Lys Gly Gly Arg Lys Val Tyr Arg Phe Lys
115 120 125
Ala Gln Gln Tyr Gly Thr Ser Trp Tyr His Ser His Phe Ser Ala Gln
130 135 140
Tyr Gly Asn Gly Val Val Gly Ala Ile Gln Ile Asn Gly Pro Ala Ser
145 150 155 160
Leu Pro Tyr Asp Thr Asp Leu Gly Val Phe Pro Ile Ser Asp Tyr Tyr
165 170 175
Tyr Ser Ser Ala Asp Glu Leu Val Glu Leu Thr Lys Asn Ser Gly Ala
180 185 190
Pro Phe Ser Asp Asn Val Leu Phe Asn Gly Thr Ala Lys His Pro Glu
195 200 205
Thr Gly Glu Gly Glu Tyr Ala Asn Val Thr Leu Thr Pro Gly Arg Arg
210 215 220
His Arg Leu Arg Leu Ile Asn Thr Ser Val Glu Asn His Phe Gln Val
225 230 235 240
Ser Leu Val Asn His Thr Met Cys Ile Ile Ala Ala Asp Met Val Pro
245 250 255
Val Asn Ala Met Thr Val Asp Ser Leu Phe Leu Gly Val Gly Gln Arg
260 265 270

	Tyr	Asp	Val	Val	Ile	Glu	Ala	Asn	Arg	Thr	Pro	Gly	Asn	Tyr	Trp	Phe	
			275						280				285				
5	Asn	Val	Thr	Phe	Gly	Gly	Gly	Leu	Leu	Cys	Gly	Gly	Ser	Arg	Asn	Pro	
		290					295					300					
	Tyr	Pro	Ala	Ala	Ile	Phe	His	Tyr	Ala	Gly	Ala	Pro	Gly	Gly	Pro	Pro	
	305					310					315					320	
10	Thr	Asp	Glu	Gly	Lys	Ala	Pro	Val	Asp	His	Asn	Cys	Leu	Asp	Leu	Pro	
					325					330					335		
	Asn	Leu	Lys	Pro	Val	Val	Ala	Arg	Asp	Val	Pro	Leu	Ser	Gly	Phe	Ala	
				340					345					350			
15	Lys	Arg	Ala	Asp	Asn	Thr	Leu	Asp	Val	Thr	Leu	Asp	Thr	Thr	Gly	Thr	
			355					360					365				
20	Pro	Leu	Phe	Val	Trp	Lys	Val	Asn	Gly	Ser	Ala	Ile	Asn	Ile	Asp	Trp	
		370					375					380					
	Gly	Arg	Ala	Val	Val	Asp	Tyr	Val	Leu	Thr	Gln	Asn	Thr	Ser	Phe	Pro	
	385					390					395					400	
25	Pro	Gly	Tyr	Asn	Ile	Val	Glu	Val	Asn	Gly	Ala	Asp	Gln	Trp	Ser	Tyr	
				405						410					415		
	Trp	Leu	Ile	Glu	Asn	Asp	Pro	Gly	Ala	Pro	Phe	Thr	Leu	Pro	His	Pro	
				420					425					430			
30	Met	His	Leu	His	Gly	His	Asp	Phe	Tyr	Val	Leu	Gly	Arg	Ser	Pro	Asp	
			435					440					445				
35	Glu	Ser	Pro	Ala	Ser	Asn	Glu	Arg	His	Val	Phe	Asp	Pro	Ala	Arg	Asp	
		450					455					460					
	Ala	Gly	Leu	Leu	Ser	Gly	Ala	Asn	Pro	Val	Arg	Arg	Asp	Val	Ser	Met	
	465					470					475					480	
40	Leu	Pro	Ala	Phe	Gly	Trp	Val	Val	Leu	Ser	Phe	Arg	Ala	Asp	Asn	Pro	
					485					490					495		
45	Gly	Ala	Trp	Leu	Phe	His	Cys	His	Ile	Ala	Trp	His	Val	Ser	Gly	Gly	
				500					505					510			
	Leu	Gly	Val	Val	Tyr	Leu	Glu	Arg	Ala	Asp	Asp	Leu	Arg	Gly	Ala	Val	
			515					520					525				
50	Ser	Asp	Ala	Asp	Ala	Asp	Asp	Leu	Asp	Arg	Leu	Cys	Ala	Asp	Trp	Arg	
		530					535					540					
55	Arg	Tyr	Trp	Pro	Thr	Asn	Pro	Tyr	Pro	Lys	Ser	Asp	Ser	Gly	Leu	Lys	
	545					550					555					560	
	His	Arg	Trp	Val	Glu	Glu	Gly	Glu	Trp	Leu	Val	Lys	Ala				
					565					570							